

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC25572A		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/IB2004/003791		International filing date (day/month/year) 19.11.2004		Priority date (day/month/year) 24.11.2003
International Patent Classification (IPC) or national classification and IPC C07D487/04, A61K31/395, A61K31/505, A61P9/12				
Applicant PFIZER LIMITED et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 09.02.2005		Date of completion of this report 14.10.2005		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Härtinger, S Telephone No. +49 89 2399-		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/003791

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-130 as originally filed

Claims, Numbers

1-15 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/003791

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-15
	No: Claims	
Inventive step (IS)	Yes: Claims	1-15
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-15
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. The application relates to 2,4-diamino pyrazolpyrimidine derivatives with cGMP-PDE-5 inhibitory activity. The compounds are therefore useful i.a. in the treatment of hypertension and male erectile dysfunction.

- D1: WO 02/00660 A (MERCK PATENT GMBH; JONAS, ROCHUS; SCHELLING, PIERRE; CHRISTADLER, MARI) 3 January 2002 (2002-01-03)
D2: US-A-6 130 223 (JONAS ET AL) 10 October 2000 (2000-10-10)
D3: DUMAITRE B ET AL: "SYNTHESIS AND CYCLIC GMP PHOSPHODIESTERASE INHIBITORY ACTIVITY OF A SERIES OF 6-PHENYLPYRAZOLO 3,4-DPYRIMIDONES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 39, no. 8, 1996, pages 1635-1644, XP000651134 ISSN: 0022-2623
D4: WO 02/102314 A (BRISTOL-MYERS SQUIBB COMPANY; VACCARO, WAYNE; ROBERGE, JACQUES, Y; LEF) 27 December 2002 (2002-12-27)
D5: EP-A-1 348 707 (USTAV EXPERIMENTALNI BOTANIKY AV CR (INSTITUTE OF EXPERIMENTAL BOTANY) 1 October 2003 (2003-10-01)

2. The present compounds of the formula (I) differ from that of D1 by the present 4-amino group, which is directly substituted with a cyclic group. With respect to D2 to D4 novelty resides from the presently fused pyrazole ring. While there appears to be a generic overlap with the compounds of D5 (see claim 1), the presently selected carboxamide fragment according to present group R5 has not been individualised (see Tables of D5). As such, the selection is considered novel.

In the light of the novelty of the present compounds, the subject-matter of all further independent claims is likewise novel, since they refer to the structural features of the compounds. ~~The claimed matter appears to have met the requirements of Art. 33(2) PCT.~~

3. Only D1 to D4 relate to products which share the utility of the present compounds.

The 4-amino pyrazolpyrimidine derivatives disclosed in D1 represent the closest prior art. In order to arrive at the subject of the present application, the skilled person would have to modify the substituents, which are bonded to positions 2, 4 and 7 of the bicyclic core. The modification would also embrace the shortening of the methylene spacers at positions 2 and 4, which however have been presented as invariable part in the prior art. By consequence, the skilled person, who was looking to solve the problem of providing further cGMP-PDE-5 inhibitors, was not guided by teaching of D1 as to the structural requirements of the product. As the description provides support that the present class of products have the desired activity (see page 130), the structural modification is considered to be a not obvious solution to the problem. The claimed matter appears to have met the requirements of Art. 33(3) PCT.

Re Item VI

Certain documents cited

1. The in international patent application D6 (= WO 2004/096810 A PFIZER LIMITED; BELL, ANDREW, SIMON; BROWN, DAVID, GRAHAM; FOX, DAVID) has been published between the priority and filing date of the present application. The 2,4-diamino pyrazolpyrimidine derivatives do therefore not belong to the prior art as defined in the PCT.

Re Item VIII

Certain observations on the international application

1. The reference to "polymorph" in claim 1 appears to be speculative and not supported by the description, as no such species are disclosed in the application nor the manner, in which they could be obtained.
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